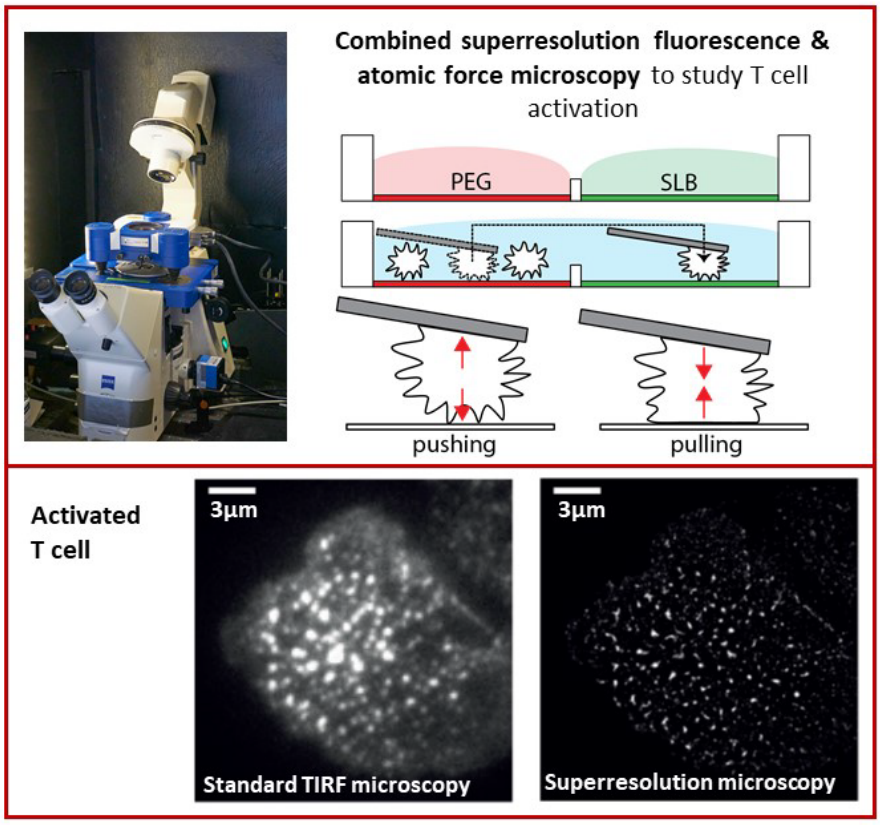
DEVELOPMENT OF AN AUTONOMOUS MICROSCOPY PLATFORM FOR ADAPTIVE EXPERIMENTATION IN CELL BIOLOGY



Supervisory Team[1]

Primary Supervisor: *Gerhard J. Schütz, Institute of Applied Physics*

TU Wien project partners: *Radu Grosu, Institute of Computer Engineering; Robert Sablatnig, Computer Vision Lab; Eva Sevcsik & Markus Valtiner, Institute of Applied Physics; Philipp Thurner, Institute of Lightweight Design and Structural Biomechanics*

External academic partners: *Jörg Enderlein, Georg-August University Göttingen; Alexander Jesacher, Medical University of Innsbruck*

External industry partners: *Sebastian Rhode, Carl Zeiss Microscopy GmbH; Max Sonnleitner, GenSpeed*

[1] The Early Stage Researchers (ESRs) will be accompanied during their thesis by an individual "Thesis Advisory Committee" (TAC), which will guide the ESR through the graduate studies. The TAC will consist of the thesis primary supervisor, and two additional members of the Supervisory Team selected by the ESR.

Project Description

Biological cells continuously explore their environment and react to biochemical and biophysical stimuli, such as the presence and spatial organization of specific ligands, but also the dynamical behavior of the matrix or its rigidity. In turn, cell-exerted processes also affect the cellular environment, e.g. due to morphological changes of the cell that impose forces on the surrounding system. Current experimental approaches hardly account for the presence of such dynamic signaling networks, as they are based on rather passive microscopy platforms. In this project, we propose to go beyond the state of the art by developing an **autonomous microcopy platform**, which enables the automated interpretation of cell biological images, and – based on a set of user-defined rules – a corresponding response exerted on the cell by the microscopy platform.

As basis for the development of the autonomous microscope, we will use a **T cell activation system** which is well established in the Schütz lab. T cells will be imaged using ultra-sensitive microscopy, which allow for superresolution microscopy (see Rossboth et al., Nature Immunology 19:821, 2018). Eventually, the student can use a combination of an atomic force microscope with fluorescence microscopy (Fölser et al., Cells 10:235, 2021).

Key Goals and Tasks

Automated cell selection. As a first step, the student will automate the selection process of the cells of interest. Low resolution overview images of appr. 10^6 cells will be analyzed using supervised learning approaches, and the chosen cells of interest will be automatically positioned in the field of view for subsequent high resolution microscopy.

Adaptive superresolution imaging. For single molecule localization microscopy, up to 10^5 images of the very same sample position need to be analyzed. Currently, however, the timing protocols do not account for changes in the sample during the recording sequence. We will account for alterations in the sample due to the imaging process, and adapt timing protocols automatically during the recording sequence to obtain a higher quality of the resulting images, particularly with respect to the final resolution obtained.

Combined force and fluorescence microscopy. In the Schütz lab, we use AFM cantilevers to position T cells close to activating surfaces in order to study the details of the cell adhesion process. Cell adhesion involves the protrusion and retraction of cellular microvilli towards the activating surface. For capturing this process it is hence critical to rapidly adjust the cantilever position, using the information of the cellular contacts as input. The student shall develop an automated hardware control system based on reinforcement learning, which enables for the first time the prolonged observation of this adhesion process.

Project-specific Requirements

- Completed master studies in (bio-)physics or a related discipline
- Expertise in microscopy and optics
- Interest in machine learning and in cell biology
- Willingness to travel to project meetings and scientific conferences
- Excellent English language skills
- Personal skills: Independence, ability to work in a team, problem-solving skills